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09/622,703	08/21/2000	Warren Hoeffler	XGEN-110-USA	8907

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/622,703	Applicant(s) HOEFFLER, WARREN
	Examiner Arun Chakrabarti	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *15-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-2, 4-8, 10, and 13 are rejected under 35 U.S.C. 102 (b) as being anticipated by Gansz et al. (Molecular and General Genetics, (1991), Vol. 225, pages 427-434).

Gansz et al teach a method of detecting transcription activity (Summary) comprising the steps of :

a) providing a DNA template comprising at least one binding region for a transcription factor (Page 428, column 1, Materials and Methods Section, DNA isolation subsection);

b) contacting the DNA template with at least one transcription factor (Figures 1 and 2 and Materials and Methods Section, Gel-retardation assay subsection);

c) detecting the presence or absence of a nick in the DNA template, wherein the presence of a nick in the DNA template indicates transcription activity (Summary, lines 11-12 and Results and Discussion section, The DsbA protein induces DNA nicking subsection and Figures 2-5).

Gansz et al teach a method wherein the presence or absence of a nick in a DNA molecule is measured by determining the change in electrophoretic mobility of nicked DNA on an electrophoretic gel by a DNA sequencing assay (Figure 5 and Materials and Methods Section, DNAse I foot printing subsection).

Gansz et al teach a method wherein the presence or absence of a nick in a DNA molecule is determined by a primer extension, polymerase chain reaction and amplification reaction (Materials and Methods Section, DNA sequencing subsection).

Gansz et al teach a method wherein the presence or absence of a nick in a DNA molecule is determined by a protein binding assay (Figure 2 and Results and Discussion section, Gel Retardation Assay subsection).

Gansz et al teach a method wherein the DNA is affixed to a gel matrix (Figures 2-5 and Materials and Methods Section, In vitro transcription assays subsection).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2, 4-10, and 13-14 are rejected under 35 U.S.C. 103 (a) over Gansz et al. (Molecular and General Genetics, (1991), Vol. 225, pages 427-434) in view of Mirzabekov et al. (U.S. Patent 5,851,772) (December 22, 1998).

Gansz et al teach the method of claims 1-2, 4-8, 10, and 13 as described above.

Gansz et al do not teach the method wherein the DNA is affixed to a biological chip.

Mirzabekov et al teach the method wherein the DNA is affixed to a biological chip. (Figures 1 and 3 and Column 2, lines 42-56).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the DNA affixed to a biological chip of Mirzabekov et al. in the method of detecting transcription activity of a DNA molecule of Gansz et al., since Mirzabekov et al. state, "Still another object of the present invention to provide an easy method for identifying and subsequently enriching specific sequences of DNA. A feature of the present invention is the ease of use of a large number of oligomers immobilized on a fractionation chip and which are complementary to the desired DNA sequences, to isolate the target sequences contained on ssDNA. An advantage of the invented method is the dramatic reduction in the required number of immobilized oligomers to pinpoint desired DNA sequences compared to typical SHOM sequencing techniques. (Column 2, lines 43-53)." An ordinary practitioner would have been motivated to combine and substitute the DNA affixed to a biological chip of Mirzabekov et al. in the method of detecting transcription activity of a DNA molecule of Gansz et al., in order to improve the transcription activity detection of a large

number of DNA molecules in a short period of time and also in order to achieve the express advantages, as noted by Mirzabekov et al, of an invention which provide an easy method for identifying and subsequently enriching specific sequences of DNA and also to exploit the ease of use of a large number of oligomers immobilized on a fractionation chip which are complementary to the desired DNA sequences, to isolate the target sequences contained on ssDNA and also to achieve the advantage of a method which provides the dramatic reduction in the required number of immobilized oligomers to pinpoint desired DNA sequences compared to typical SHOM sequencing techniques.

5. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 103 (a) over Gansz et al. (Molecular and General Genetics, (1991), Vol. 225, pages 427-434) in view of Hodgson et al. (U.S. Patent 5,854,020) (December 29, 1998).

Gansz et al teach the method of claims 1-2, 4-8, 10, and 13 as described above.

Gansz et al do not teach the method wherein the transcription initiation site is determined by S1 nuclease assay.

Hodgson et al teach the method wherein the transcription initiation site is determined by S1 nuclease assay (Column 5, lines 21-25).

Gansz et al do not teach the method wherein the transcription factor is in a nuclear cell extract.

Hodgson et al teach the method wherein the transcription factor is in a nuclear cell extract (Column 19, lines 10-19).

Gansz et al do not teach the method wherein the DNA template is inserted into a viral or plasmid vector and introduced in a cell.

Hodgson et al teach the method wherein the DNA template is inserted into a viral or plasmid vector and introduced in a cell (Column 19, lines 14-24).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the transcription initiation site determination by S1 nuclease assay and viral or plasmid vector as well as using the transcription factor from a nuclear cell extract of Hodgson et al. in the method of detecting transcription activity of a DNA molecule of Gansz et al., since Hodgson et al. state, "Within the promoter sequence will be found a transcription initiation site conveniently defined by mapping with nuclease S. (Column 5, lines 22-24)." An ordinary practitioner would have been motivated to combine and substitute the transcription initiation site determination by S1 nuclease assay of Hodgson et al. in the method of detecting transcription activity of a DNA molecule of Gansz et al., in order to improve the transcription activity detection and also in order to achieve the express advantages, as noted by Hodgson et al, of mapping with nuclease S1 which conveniently define transcription initiation site.

Response to Arguments

6. Applicant's arguments filed on April 5, 2002 have been fully considered but they are not persuasive.

Applicant argues that 102 (b) rejection based on Gansz et al. (Molecular and General Genetics, (1991), Vol. 225, pages 427-434) should be withdrawn because no positive correlation between nicking of DNA and transcription has been demonstrated by the reference. This argument is not persuasive. Applicant argues that Gansz et al. reference does not teach the correlation between nicking of DNA and transcription of the claimed invention. Applicant argues that the word "correlation between nicking of DNA and transcription" was not found in Gansz reference and only the words "have no explanation" and "might be responsible" are found. Applicant argues that because Gansz has a preferred embodiment of speculation, Gansz is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Gansz has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Gansz reference uses speculative terms e.g., "might be responsible" or "might contribute" to explain the results of their invention, the property of transcription as a result of nicking is inherently present in this chemically and structurally identical molecule. For example, Gansz reference clearly teaches that such nicks "contribute to activation of the template for late transcription" (Page 428,

column 1, lines 6-7). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)". In this case, any nicks of DNA under any suitable conditions can be attributed to the transcription as clearly taught and suggested by Gansz.

However, in response to argument, claims 11 and 12 has been withdrawn from 102 (b) rejection and has been replaced by 103 (a) rejection based on the same reference of Hodgson as cited in the last office action.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is lack of motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Hodgson et al. since Hodgson et al. state, "Within the promoter sequence will be found a transcription initiation site conveniently defined by mapping with nuclease S. (Column 5, lines 22-24)." This logic is applicable to other 103 (a) rejection as well.

Applicant then argues the 103 rejection is improper because it lacks a reasonable expectation of success.

With regard to the "lack of reasonable expectation of success", the MPEP 2143.02 states "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Gansz reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different nicks in the DNA of T4 bacteriophage were actually experimentally studied and found to be functional to enhance transcription (Abstract and Page 428, column 1, lines 2-7). This evidence of functionality trumps the attorney arguments, which argues that Gansz reference is an invitation to research, since Gansz steps beyond research and shows the functional product.

In view of the response to argument, all rejections as made in the last office action are hereby properly maintained.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W.Gary Jones, can be reached on (703)308-1152.

Any inquiry of general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703)605-1237.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti,

Patent Examiner

Art Unit 1634

May 28, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600